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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/768,877	01/23/2001	Kenneth S. Polonsky	ARCD:307USD1	4378

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EXAMINER

RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 03/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/768,877

Applicant(s)

POLONSKY ET AL.

Examiner

Delia M. Ramirez

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 January 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 18-21 and 49-114 is/are pending in the application.
- 4a) Of the above claim(s) 65-113 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 18-21, 49-51, 53-64 and 114 is/are rejected.
- 7) ☒ Claim(s) 52 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 January 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Claims 18-21, 49-114 are pending.

Applicant's amendment of claims 18-21, 50-55 and 56-60, addition of claim 114 and amendments to the specification in Paper No. 15, filed on 1/21/2003 are acknowledged.

As indicated in previous Office Action Paper No. 14, mailed on 10/16/2002, claims 65-113 were withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to an invention non-elected without traverse in Paper No. 11, filed 4/16/2002. A complete reply to the final rejection must include cancellation of non-elected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Information Disclosure Statement

1. A copy of the information disclosure statement (IDS) first submitted on 3/26/2001 is acknowledged. It is noted that references C28-C29 do not provide the corresponding EMBL accession number or the publication date. The XP number in those references is not an EMBL number. As such, they have not been considered by the Examiner. The remaining references have been considered by the Examiner.

Drawings

2. The formal drawings submitted on 1/21/2003 have been reviewed and are approved by a draftsman under 37 CFR 1.84 or 1.152.

Claim Rejections - 35 USC § 112, Second Paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 18-21, 49-51, 53-64 and 114 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claims 18-21 and 54 were found indefinite due to the recitation of "standard activity profile".

6. This rejection, as it relates to claims 18-21 and 54, has been discussed at length in Paper No. 14, mailed on 10/16/2002. It is now applied to newly added claim 114 for the reasons of record.

7. It is noted that claim 57 was inadvertently included in the list of rejected claims in Paper No. 14.

8. Applicants argue that the specification discloses that the standard activity profile of the calpain 10 polypeptide may be determined by measuring the binding of the calpain 10 polypeptide to a synthetic substrate. Applicants further assert that claims 49 and 55 limit claims 18 and 54, respectively since they indicate how the standard activity profile is determined.

Art Unit: 1652

9. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. The specification fails to define the term itself and there is no definition of the term "standard" as it relates to an activity profile. As indicated in previous Office Action Paper No. 14, an activity profile will be different depending on the conditions chosen to measure such activity. As such, there is no known "standard activity profile" and one of skill in the art would not necessarily be appraised of which are the "standard" conditions used to obtain an activity profile of calpain 10. While it is agreed that the specification in page 7, lines 17-19, describes that the standard activity profile may be determined by measuring the binding of the calpain 10 polypeptide to a synthetic substrate, the specification appears to indicate that there are other ways (i.e. different conditions) to determine the standard activity profile in addition to measuring the binding of the calpain 10 to a synthetic substrate. The Examiner acknowledges that claims 49 and 55 further limit claims 18 and 54 in regard to the "standard activity profile", which is the reason why this rejection was not applied to claims 49 and 55, however, claims 18 and 54 (claims 19-21 and 114 dependent thereon) are indefinite since they do not contain this limitation. The Examiner provided in Paper No. 14 suggested language which may overcome the instant rejection. Correction is required.

10. Claims 18-21, 49, 51, 53-55, 57-60 (claims 50, 56, 61-64 dependent thereon) are indefinite in the recitation of "calpain 10" for the following reasons. While the specification discloses that a calpain 10 is an atypical calpain and that it is similar in structural organization to calpain 5 and 6, it is unclear as to which are the characteristics which are unique to a polypeptide having "calpain 10" function which would allow one of skill in the art to clearly differentiate a calpain 10 from other calpains, particularly calpains 5 and 6. Furthermore, while one could

Art Unit: 1652

argue that the term "calpain 10" may be defined in regard to humans and possibly mouse, the term encompasses any calpain 10 from any source. Since there is no disclosure in regard to specific structural and functional characteristics which are unique to calpain 10 polypeptides, one of skill in the art cannot reasonably apprise of the scope of the invention. Correction is required.

11. Claim 53 is indefinite in the recitation of "the method of claim 52 wherein the calpain 10 polypeptide has a sequence comprising amino acid 1-47 of SEQ ID NO: 2" since it does not further limit claim 52. It is noted that the genus of polypeptides comprising amino acids 1-47 of SEQ ID NO: 2 encompasses the subgenus of polypeptides comprising the polypeptide of SEQ ID NO: 2. Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 19, 49, 53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 19 and 53 (claim 49 dependent thereon) has been amended to encompass a method of screening for a modulator of calpain 10 function wherein the calpain 10 polypeptide used comprises amino acids 1-47 of SEQ ID NO: 2. While the specification discloses a method

Art Unit: 1652

as described above wherein the calpain 10 polypeptide used is that of SEQ ID NO: 2, the Examiner is unable to locate adequate support in the specification for a method of screening for a modulator of calpain 10 function with a calpain 10 polypeptide which comprises specifically amino acids 1-47 of SEQ ID NO: 2. Furthermore, the Examiner has not been able to find a specific reference to amino acids 1-47 of SEQ ID NO: 2. Thus there is no indication that methods using specifically calpain 10 polypeptides which comprise amino acids 1-47 of SEQ ID NO: 2 were within the scope of the invention as conceived by Applicants at the time the application was filed. Accordingly, Applicants are required to cancel the new matter in the response to this Office Action.

14. Claims 18-21, 49-51, 53-64 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

15. This rejection was discussed at length in Paper No. 14, mailed on 10/16/2002 and it is applied to amended claim 53 for the reasons of record.

16. Applicants argue that the claims as amended now recite "calpain 10". As such, it is Applicant's opinion that the specification has provided enough description of calpain 10. Applicants point out the description provided in Table 1, Figure 1, Figure 5, Figure 6, Example 8, and the structure of several isoforms of calpain 10. Therefore, Applicants conclude that one of skill in the art could clearly see that Applicants were in possession of the claimed invention at the time of filing.

Art Unit: 1652

17. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. While the Examiner agrees that the specification provides the structure of several human calpain 10 polypeptides and one mouse calpain 10, the species described are not considered sufficient to describe the entire genus of calpain 10 polypeptides required to practice the claimed method. Applicants assert that the specification (page 31, lines 8-10) provides description of structural elements which are indicative of calpain 10 function. It is noted however that the structural description provided is also relevant to calpain 5 and 6, therefore one cannot find sufficient description of the critical structural elements which are specific to all calpain 10 polypeptides. It is also noted that there is no disclosure in the specification of how amino acids 1-47 of the polypeptide of SEQ ID NO: 2 correlate with calpain 10 activity. While one could argue that the genus of calpain 10 polypeptides required to practice the claimed method are adequately described since one could isolate other calpain 10 polypeptides by structural homology, as indicated previously, the state of the art teaches the unpredictability of assigning function based on structural homology. See the teachings of Bork (Genome Research, 10:398-400, 2000), Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995) and Broun et al. (Science 282:1315-1317, 1998) already discussed. Further examples of how minimal changes in structure can lead to polypeptides of different functions are shown by Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) and Witkowski et al. (Biochemistry 38:11643-11650, 1999). Witkowski et al. teaches that one amino acid substitution transforms a β -ketoacyl synthase into a malonyl decarboxylase and completely eliminates β -ketoacyl synthase activity. Seffernick et al. teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and

Art Unit: 1652

dehalogenation, therefore having different function. The specification only discloses a few species of the genus of calpain 10 polypeptides which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of all species within the genus required to practice the claimed method. Thus, one skilled in the art cannot reasonably conclude that Applicant had possession of the claimed invention at the time the instant application was filed.

18. Claims 18-21, 49-51, 53-64 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of screening for inhibitors of the human calpain 10 polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for a method of screening for inhibitors of (1) any calpain 10 polypeptide or (2) any calpain 10 polypeptide comprising amino acids 1-47 of the polypeptide of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

19. This rejection has been discussed at length in Paper No. 14, mailed on 10/16/2002 and it is applied to the amended claims for the reasons of record.

20. Applicants argue that the specification provides ample teaching with respect to a calpain 10 polypeptide. Applicants assert that the specification discloses several calpain 10 isoforms in Table 1, Figure 1, Figure 5, and that several working examples have been provided in pages 123-165 which show how to make and use the invention, such as in detecting and analyzing polymorphisms in individuals. It is Applicant's opinion that the specification provides relevant teachings in regard to characteristics and functionality of calpain 10 and its isoforms.

Art Unit: 1652

21. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. The Examiner acknowledges the disclosure of several human calpain 10 isoforms, one mouse calpain 10 as well as the working examples provided. It is noted however that the claims as amended are directed to a method of screening for inhibitors of any (i.e. from any source) calpain 10 polypeptide. As indicated previously, the specification fails to disclose critical structural elements which are specific to all calpain 10 polypeptides. See discussion above in regard to the structural description provided by the specification. In addition, the specification fails to disclose how amino acids 1-47 of the polypeptide of SEQ ID NO: 2 correlate with calpain 10 function. Therefore, it is unclear if polypeptides comprising amino acids 1-47 of the polypeptide of SEQ ID NO: 2 will display calpain 10 function.

While one could argue that any calpain 10 polypeptide required to practice the claimed method can be isolated by structural homology, as indicated previously, the state of the art teaches the unpredictability of assigning function based on structural homology as evidenced by Bork, Van de Loo et al., Broun et al., Seffernick et al. and Witkowski et al., already discussed. Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge about the critical structural elements required to display calpain 10 function, and the unpredictability of the prior art in regard to function based on homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to isolate calpain 10 polypeptides and practice the claimed method. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to practice the full scope of the claimed invention.

Claim Rejections - 35 USC § 102

22. Claims 18, 20-21, 51, 54, 58-60 were rejected under 35 U.S.C. 102(b) as being anticipated by Meyer et al. (Biochem. J. 314:511-519, 1996).
23. This rejection has been discussed at length in Paper No. 14, mailed on 10/16/2002.
24. Applicants argue that the claims now recite "calpain 10" therefore, since Meyer et al. does not teach a method of screening for a modulator of calpain 10, the instant reference does not anticipate the claims.
25. In view of Applicant's amendment to the claims, which now recite "calpain 10", this rejection is hereby withdrawn since Meyer et al. teach a method for screening modulators of calpain I.

Allowable Subject Matter

26. Claim 52 appears to be allowable over the prior art of record but it is objected to since it depends upon a rejected claim. It would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

27. No claim is in condition for allowance.
28. Applicant's amendment of claims 18-21, 50-55, 56-60 and addition of claim 114 necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Art Unit: 1652

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

29. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

30. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

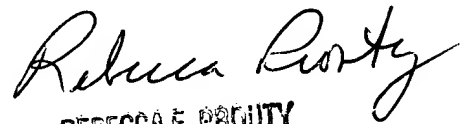
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

Art Unit: 1652

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
March 21, 2003


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1600